

## Public health and policy

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### Abstract

Antimicrobial agent usage data are essential for focusing efforts to reduce misuse and overuse of antimicrobial agents in food producing animals because these practices may select for resistance in bacteria of animals. Transfer of resistant bacteria from animals to humans can lead to human infection caused by resistant pathogens. Resistant infections can lead to treatment failures, resulting in prolonged or more severe illness. Multiple World Health Organization (WHO) reports have concluded that both antimicrobial resistance and antimicrobial usage should be monitored on the national level. The system for collecting antimicrobial usage data should be clear and transparent to facilitate trend analysis and comparison within and among countries. Therapeutic, prophylactic and growth promotion use should be recorded, along with route of administration and animal species and/or production class treated. The usage data should be compared to resistance data, and the comparison should be made available in a timely manner. In the United States, surveillance of antimicrobial resistance in foodborne bacteria is performed by the National Antimicrobial Resistance Monitoring System (NARMS) for enteric bacteria, however, the United States still lacks a mechanism for collecting antimicrobial usage data. Combined with antimicrobial resistance information from NARMS, antimicrobial usage data will help to direct education efforts and policy decisions, minimizing the risk that people will develop antimicrobial resistant infections as a result of eating food of animal origin. Ultimately mitigation strategies guided by usage data will be more effective in maintaining antimicrobial drugs for appropriate veterinary use and in protecting human health.

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Data on usage of antimicrobial agents are essential for focusing efforts to reduce misuse and overuse of antimicrobial agents in food producing animals. Reducing the misuse and overuse of antimicrobial agents in food animals is important in reducing selective pressures which lead to development of resistance in bacteria and dissemination of resistant bacteria in the gastrointestinal tracts of animals and in farm environments. These resistant bacteria can be transferred to humans through direct contact with animals or through consumption of contaminated food or water. Transfer of resistant bacteria to humans can lead to human infection caused by resistant pathogens. Resistant infections can lead to treatment failures, resulting in prolonged or more severe illness. Even those bacteria that are not pathogenic to humans may bring along mobile resistance genes, which can be passed on to human bacterial pathogens (Angulo et al., 2000; Anderson et al., 2003).

The adverse human health consequences of antimicrobial use in food-producing animals were highlighted by the international public health community at a meeting held by the World Health Organization (WHO) in Berlin, in October 1997. This meeting of experts, entitled “The Medical Impact of the Use of Antimicrobials in Food Animals”, acknowledged that antimicrobial use can select resistant forms of bacteria. The Berlin meeting also acknowledged that resistant bacteria and resistance genes can be exchanged between humans, animals, and the environment. Given these acknowledgements, experts at the 1997 meeting concluded that both antimicrobial resistance and antimicrobial usage should be monitored on a national level (World Health Organization, 1997). Furthermore, amongst the Berlin meeting recommendations intended to mitigate the consequences of using antimicrobials in food-producing animals was the recommendation that the WHO arrange an expert consultation to develop a code of practice for prudent use of antimicrobials in food animal production (World Health Organization, 1997).

The WHO subsequently convened a meeting in Geneva in June 2000 to develop principles for minimizing the negative public health impact of the use of antimicrobial agents in food-producing animals while also providing for the safe and effective use of antimicrobials in veterinary medicine. Published as the “WHO Global Principles for the Containment of Antimicrobial Resistance in Animals Intended for Food”, these Principles are intended to help reduce the misuse and overuse of antimicrobials in animals intended for food. The Principles, which cover responsibilities of many stakeholder groups, call for surveillance of antimicrobial resistance and usage (World Health Organization, 2000).

The Global Principles for the Containment of Antimicrobial Resistance in Animals Intended for Food recognize antimicrobial usage data, along with resistance data, as “essential” in developing national policies, pre- and post-licensing processes and treatment guidelines for veterinary use (World Health Organization, 2000). The need for monitoring the use of antimicrobials in food animals was further emphasized by a consultation meeting in Oslo, Norway in September 2001. The report from the consultation, “Monitoring Antimicrobial Usage in Food Animals for the Protection of Human Health” provides recommendations to support governments, national authorities, and various other stakeholders in establishing national monitoring systems to collect food animal production antimicrobial usage data (World Health Organization, 2001). The system for collecting antimicrobial usage data should be clear and transparent to facilitate trend analysis and comparison within and among countries. Therapeutic, prophylactic and

growth promotion use should be recorded, along with route of administration and animal species and/or production class treated. The usage data should be compared to resistance data, and the comparison should be made available in a timely manner (World Health Organization, 2001). Food animal usage data are available on the websites for several European countries, including Denmark (<http://vetstat.vetinst.dk>) and the United Kingdom (<http://www.vmd.gov.uk/>).

In the United States, surveillance of antimicrobial resistance in foodborne bacteria is performed by the National Antimicrobial Resistance Monitoring System for enteric bacteria (NARMS). Established in 1996 by the Food and Drug Administration (FDA), the Centers for Disease Control and Prevention (CDC), and the U.S. Department of Agriculture (USDA), NARMS monitors changes in antimicrobial resistance in human enteric bacterial pathogens. In 1996, NARMS began standardized susceptibility testing of isolates, specifically non-Typhi *Salmonella* and *Escherichia coli* O157, from human clinical specimens at the CDC. Animal clinical specimens, specimens from healthy farm animals, and specimens from animals slaughtered for food are tested by the same microbiologic methods at the USDA. The human arm began with 14 health departments and has now grown to include all fifty states. In 1997 and 1998, *Campylobacter* surveillance was initiated in the human and animal arms, respectively (Tollefson et al., 1998). Surveillance of retail food specimens was added to NARMS in 2002. Despite the improvement and expansion of antimicrobial resistance monitoring, the United States still lacks a mechanism for collecting antimicrobial usage data. Without usage data, targeting effective intervention strategies is difficult even if increasing resistance is detected by surveillance.

Collection of usage data as set forth in the Oslo guidelines would allow the United States to contribute more fully to the global effort to contain antimicrobial resistance in animals intended for food. Collection of antimicrobial usage information is also important for use by public health and regulatory systems within the United States. Combined with antimicrobial resistance information from NARMS, antimicrobial usage data will help to direct education efforts and policy decisions, minimizing the risk that people will develop antimicrobial resistant infections as a result of eating food of animal origin. Ultimately mitigation strategies guided by usage data will be more effective in maintaining antimicrobial drugs for appropriate veterinary use and in protecting human health.

Monitoring of antimicrobial usage in animals intended for food animals at the national level, would better enable the FDA to track and evaluate the development of antimicrobial resistance and to target mitigation strategies to prolong the effectiveness of animal drugs and protect human health. The merging of resistance data from NARMS with usage data would enable the FDA to estimate associations between antimicrobial resistance and antimicrobial use and identify changes that could prevent or slow the spread of the development of antimicrobial resistance. For example, educational efforts could be targeted to reduce use that is judged by appropriate groups to be improper or unnecessary and might be shown to promote the development of antimicrobial resistance. For regulatory purposes, usage data would help identify antimicrobials for which development of resistance is most likely and identify potential co-resistance (i.e. between different classes of antimicrobials), thus assisting the FDA in refining pre-approval processes for

antimicrobial drugs intended for use in food animals. In addition, some specific applications of usage data might include quantitative risk assessments and development of recommendations to the USDA Food Safety Inspection Services (FSIS) for improvement of the residue prevention system.

Information on antimicrobial drug use in human medicine is available through proprietary sources of human prescription data, and increasingly through national public health surveillance at the CDC's National Center for Health Statistics. The usefulness of data gathered through NCHS's National Ambulatory Medical Care Survey (NAMCS) is described in the 2002 JAMA article "Trends in antimicrobial prescribing rates for children and adolescents" (McCaig et al., 2002). NAMCS data on prescribing practices of office-based physicians provides information to help target interventions promoting appropriate antimicrobial use and to help evaluate effectiveness of intervention efforts. NCHS also conducts the National Hospital Ambulatory Medical Care Survey (NHAMCS), a major source of data on drug prescribing by hospital outpatient and emergency departments. Inpatient data are more difficult to collect. However, the National Nursing Home Survey has collected limited drug use information in the past and will collect more information on future surveys. Also, the National Hospital Discharge Survey is studying the feasibility of collecting drug use data on hospital patients.

Arlington Medical Resources Inc., IMS Health Inc., and Verispan are companies whose data systems are typically designed for industrial clients such as the pharmaceutical industry although their data have been purchased and used for public health purposes by the FDA and others. Drug use surveillance data for human medicine in Europe is available at [www.us.ac.be/ESAC](http://www.us.ac.be/ESAC) and contains data for 1997–2001 from 27 countries.

In conclusion, the World Health Organization has repeatedly concluded that data on usage of antimicrobial agents are essential for focusing efforts to reduce misuse and overuse of antimicrobial agents. Data on usage of antimicrobial agents in humans medicine is available in the United States. Data on usage of antimicrobial agents in food animals in the United States, however, is not currently available. The absence of such data is particularly notable in the light of the recent marked enhancements in national surveillance for antimicrobial resistance in foodborne bacteria in the United States, and increasing availability of data on usage of antimicrobial agents in food animals in other countries.

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